UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,866	09/27/2005	David George Allen	P33108	2052

20462 7590 12/17/2007

SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER	
RAHMANI, NILOOFAR	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
12/17/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	10/527,866	ALLEN ET AL.	
	Examiner	Art Unit	
	Niloofar Rahmani	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51,56-60,62,63 and 68-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-51,56-60,62,63 and 68-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-51, 56-60, 62-63, and 68-71 are pending and claims 52-55, 61, 64-67, and 72-74 are cancelled in the instant application.

2. ***Priority***

This application was filed on 09/27/2005, which is a 371 of PCT/EP03/11814, filed on 09/12/2003, and claims priority of UNITED KINGDOM 0221455.9, filed on 09/16/2002, and UNITED KINGDOM 0230045.7, filed on 12/23/2002, and UNITED KINGDOM 0306595.0, filed on 03/21/2003, and UNITED KINGDOM 0308017.3, filed on 04/07/2003, and UNITED KINGDOM 0319708.4, filed on 08/21/2003, and UNITED KINGDOM 0321074.7, filed on 09/09/2003.

3. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56-60, 62-63, and 68-71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy

the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims.
2) The nature of the invention,
3) The state of the prior art,
4) The level of one of ordinary skill,
5) The level of predictability in the art,
6) The amount of direction provided by the inventor,
7) The existence of working examples,
8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn to method of treatment of an inflammatory and allergic disease or cognitive impairment in a mammal such as a human using the compound of formula (I).

The state of the prior art: " We recently reported that CD4+ T cells that have been activated in vivo or in vitro contain elevated cyclic adenosine monophosphate (cAMP) phosphodiesterase (PDE) activity. Since both phosphodiesterase inhibitors and glucocorticoids have anti-inflammatory activity,

we sought to invenstigate the effect of beclomethasone on pDE activity. In conclusion, we have shown that beclomethasone decreases PDE activity in CD4+ T cells where it has been elevated by in vitro or in vivo stimulation. In comparison, this glucocorticoid has no effect on PDE activity in CD4+ T cells from nonatopic, pre-seasonal or early-season allergic rhinitic, or even asymptomatic asthmatic, donors. The conection between glucocorticoids and cellular PDE activity appears to be coplex and merits further investigation."(Crocker et al., Allergy Immunology, 2000, Vol. 121, pages 151-160.)

The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that

in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be used for treating inflammatory disease.

Amount of guidance/working examples: On pages 74-85 of the specification, applicant has examples of test compounds and PDE4 inhibitors. However, the specification does not seem to enable the activity of compounds to a disease such as inflammatory disease or cognitive impairment.

The breadth of the claims: The breadth of claims is drawn to method of treatment of an inflammatory and allergic disease or cognitive impairment in a mammal such as a human using the compound of formula (I).

The quantity of undue experimentation needed: Since the guidance and teaching provided by the specification is insufficient for treating disease associated with PDE4 inhibitors, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claims 56-60, 62-63, and 68-71, for treating inflammatory disease or cognitive impairment, have been enabled by the instant specification.

4. Claims 56-60, 62-63, and 68-71 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being possibly enabling for treating specific diseases, does not reasonably provide enablement for preventing diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the compounds such as present here. In addition, it is presumed that "prevention" of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases

requires identifying those patients who will acquire the disease before *** occurs. This would require extensive and potentially opened ended clinical research on healthy subjects. 2) The passage spanning line 16, page 60 to line 12, page 61lists the diseases Applicant intend to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to medical treatment and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become afflicted with diseases before the fact. 6) The artisan using Applicants invention would be a Board Certified physician who specialized to treat diseases with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of inflammatory diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent inflammatory diseases generally. That is, the skill is so low that no compound effective generally against inflammatory diseases has ever been found let alone one that can prevent such conditions. 7) It is well established that "the scope of

enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by Formula (I).

The Examiner suggests deletion of the word "prevention".

5. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 63, and 68-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 63, and 68-71 are rejected because the term " A composition" is confusing. Are they claiming "Pharmaceutical composition" or "method for treatment"? Correction is required.

6. ***Claim Rejections - Obvious Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 168 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b).

Effective January 1,1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-51, 56-60, 62-63, and 68-71 are provisionally rejected under the judicially created doctrine obviousness-type double patenting as being unpatentable over the claims 73-136 of Allen et al., US 2007/0111995. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current invention embraces the invention claimed in the above patent.

Determination of the scope and content of the prior art (MPEP §2141.01)

Allen et al. of US 2007/0111995 claimed identical compounds, pharmaceutical composition, and method of using the compounds in claims 73-136 as the instant claims 1-51, 56-60, 62-63, and 68-71.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the issued claims is the claims are not word for word identical but the scope of both sets of claims overlaps mostly significantly with each other.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

The issued claims 73-136 of US 2007/0111995 are therefore fully embraced by the instant claims 1-51, 56-60, 62-63, and 68-71.

This is provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been issued.

7. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

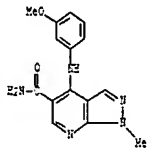
A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 8-16, 19, 31-34, 36-37 are rejected under 35 U.S.C. 102(a) as being anticipated by Nakai et al., JP 2002-20386. Nakai et al. disclosed the instant claimed compound ,which from the STN search is

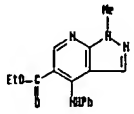
RN 389058-31-5
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxamide, 4-[(3-methoxyphenyl)amino]-1-methyl-



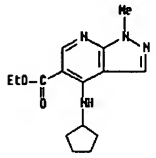
. Therefore, the instant claim is anticipated by Nakai et al.

8. Claims 1-5, 8-16, 19, 31-34, 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Dan Shi et al., Drug Development Research, 1997, Vol. 42, pages 41-56. Dan Shi et al. disclosed the instant claimed compound ,which from the STN search is

RN 160034-50-4
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-methyl-4-(phenylamino)-,ethyl ester



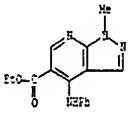
RN 160034-53-7
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-(cyclopentylamino)-1-methyl-, ethyl ester



Therefore, the instant claim is anticipated by Dan Shi et al.

9. Claims 1-5, 8-16, 19, 31-34, 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Siddiqi et al., Nucleosides & Nucleotides, 1996, Vol. 15, pages 693-717. Siddiqi et al. disclosed the instant claimed compound ,which from the STN search is

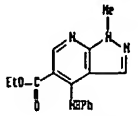
RN 160034-50-4
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-methyl-4-(phenylamino)-, ethyl ester



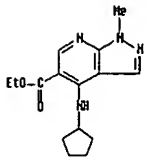
. Therefore, the instant claim is anticipated by Siddiqi et al.

10. Claims 1-5, 8-16, 19, 31-34, 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Daly et al., Medicinal Chemistry Research,1994, Vol. 4, pages 293-306. Daly et al. disclosed the instant claimed compound ,which from the STN search is

RN 160034-50-4
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-methyl-4-(phenylamino)-,ethyl ester



RN 160034-53-7
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-(cyclopentylamino)-1-methyl-, ethyl ester

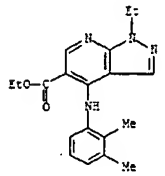


. Therefore, the instant claim is anticipated by Daly et al.

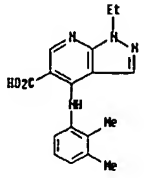
11. Claims 1-16, 19, 31-34, 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoehn et al., US 3,925,388. Hoehn et al. disclosed the instant claimed compound ,which from the STN search is

RN 34966-35-3

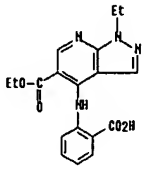
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2,3-dimethylphenyl)amino]-1-ethyl-, ethyl ester



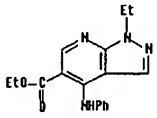
RN 34966-36-4
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2,3-dimethylphenyl)amino]-1-ethyl-



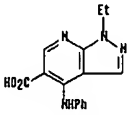
RN 34966-37-5
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2-carboxyphenyl)amino]-1- ethyl-, 5-ethyl ester



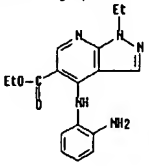
RN 34966-42-2
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-(phenylamino)-,ethyl ester



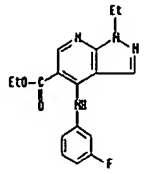
RN 34966-43-3
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-(phenylamino)-



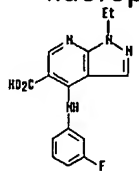
RN 53064-94-1
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2-aminophenyl)amino]-1- ethyl-, ethyl ester



RN 59444-08-5
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[(3-fluorophenyl)amino]-, ethyl ester



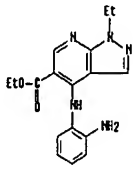
RN 59444-09-6
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[(3-fluorophenyl)amino]



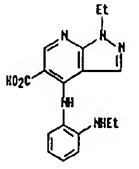
Therefore, the instant claim is anticipated by Hoehn et al.

12. Claims 1-16, 19, 31-34, 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Denzel etal., US 4,012,373. Denzel et al. disclosed the instant claimed compound ,which from the STN search is

RN 53064-94-1
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2-aminophenyl)amino]-1-ethyl-, ethyl ester

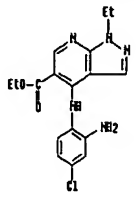


RN 53064-99-6
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[[2-(ethylamino)phenyl]amino]-

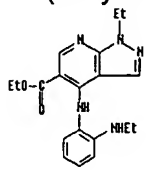


RN 53065-03-5

CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2-amino-4-chlorophenyl)amino]-1-ethyl-, ethyl ester

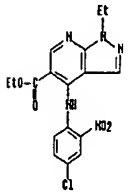


RN 53064-98-5
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[[2-(ethylamino)phenyl]amino]-, ethyl ester



RN 53065-02-4

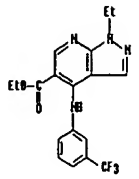
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(4-chloro-2-nitrophenyl)amino]-1-ethyl-, ethyl ester



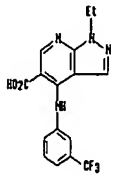
. Therefore, the instant claim is anticipated by Denzel et al.

13. Claims 1-16, 19, 31-34, 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoen et al., Journal of Heterocyclic Chemistry, 1972, Vol. 9, pages 235-53. Hoen et al. disclosed the instant claimed compound ,which from the STN search is

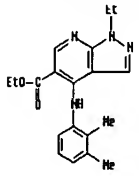
RN 34966-22-8
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[[3-(trifluoromethyl)phenyl]amino]-, ethyl ester



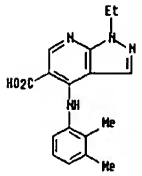
RN 34966-23-9
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[[3-(trifluoromethyl)phenyl]amino]



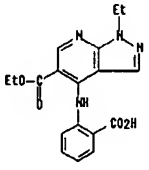
RN 34966-35-3
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2,3-dimethylphenyl)amino]-1-ethyl-, ethyl ester



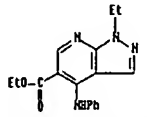
RN 34966-36-4
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2,3-dimethylphenyl)amino]-1-ethyl



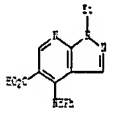
RN 34966-37-5
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2-carboxyphenyl)amino]-1-ethyl-, 5-ethyl ester



RN 34966-42-2
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-(phenylamino)-,ethyl ester



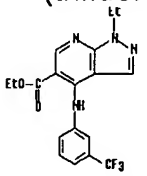
RN 34966-43-3
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-(phenylamino)-



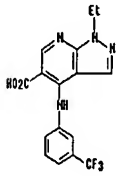
. Therefore, the instant claim is anticipated by Hoen et al.

14. Claims 1-16, 19, 31-34, 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoen et al., DE 2123318. Hoen et al. disclosed the instant claimed compound ,which from the STN search is

RN 34966-22-8
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[[3-(trifluoromethyl)phenyl]amino]-, ethyl ester

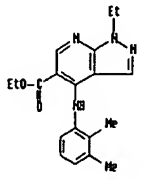


RN 34966-23-9
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[[3-(trifluoromethyl)phenyl]amino]

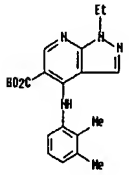


RN 34966-35-3

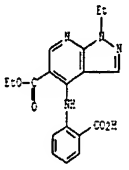
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2,3-dimethylphenyl)amino]-1-ethyl-, ethyl ester



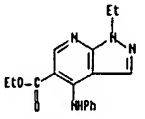
RN 34966-36-4
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2,3-dimethylphenyl)amino]-1-ethyl-



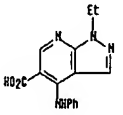
RN 34966-37-5
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-[(2-carboxyphenyl)amino]-1-ethyl-, 5-ethyl ester



RN 34966-42-2
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-(phenylamino)-,ethyl ester



RN 34966-43-3
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-(phenylamino)-



. Therefore, the instant claim is anticipated by Hoen et al.

15. ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

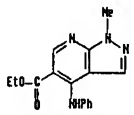
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 6-7 are rejected under 103(a) as being unpatentable over Dan Shi et al., Drug Development Research, 1997, Vol. 42, pages 41-56.

Determination of the scope and content of the prior art (MPEP §2141.01)

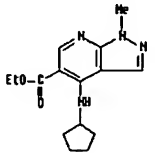
Dan Shi et al. discosed analogous compound, which from the STN search is

RN 160034-50-4
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-methyl-4-(phenylamino)-,ethyl ester



RN 160034-53-7
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-(cyclopentylamino)-1-

methyl-, ethyl ester



Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art compound is that the instant claims has R^1 being ethyl, n-propyl instead of the prior art compounds has methyl.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

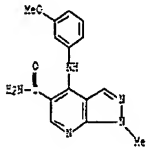
One having ordinary skill in the art would be motivated to modify the compound of Dan Shi et al. to obtain the instant compounds. Because Compounds that differ only by the presence or absence of an extra methylene group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methylene groups. See *In re Wood,* 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.

16. Claims 6-7 are rejected under 103(a) as being unpatentable over Nakai et al., JP 2002-20386.

Determination of the scope and content of the prior art (MPEP §2141.01)

Nakai et al. discosed analogous compound, which from the STN search is

RN 389058-31-5
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxamide, 4-[(3-methoxyphenyl)amino]-1-methyl-



Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art compound is that the instant claims has R^1 being ethyl, n-propyl instead of the prior art compounds has methyl.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

One having ordinary skill in the art would be motivated to modify the compound of Nakai et al. to obtain the instant compounds. Because Compounds that differ only by the presence or absence of an extra methylene group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in

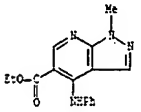
the absence of a specific teaching to add or remove methylene groups. See *In re Wood,* 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.

17. Claims 6-7 are rejected under 103(a) as being unpatentable over Siddiqi et al., Nucleosides & Nucleotides, 1996, Vol. 15, pages 693-717.

Determination of the scope and content of the prior art (MPEP §2141.01)

Siddiqi et al. discosed analogous compound, which from the STN search is

RN 160034-50-4
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-methyl-4-(phenylamino)-, ethyl ester



Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art compound is that the instant claims has R^1 being ethyl, n-propyl instead of the prior art compounds has methyl.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

One having ordinary skill in the art would be motivated to modify the compound of Siddiqi et al. to obtain the instant compounds. Because Compounds that differ only by the presence or absence of an extra methylene group or two are homologues. Homologues are of such close structural similarity

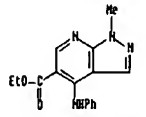
that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methylene groups. See *In re Wood,* 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.

18. Claims 6-7 are rejected under 103(a) as being unpatentable over Daly et al., Medicinal Chemistry Research,1994, Vol. 4, pages 293-306.

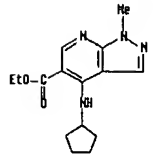
Determination of the scope and content of the prior art (MPEP §2141.01)

Daly et al. discosed analogous compound, which from the STN search is

RN 160034-50-4
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-methyl-4-(phenylamino)-,ethyl ester



RN 160034-53-7
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 4-(cyclopentylamino)-1-methyl-, ethyl ester



Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art compound is that the instant claims has R^1 being ethyl, n-propyl instead of the prior art compounds has methyl.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

One having ordinary skill in the art would be motivated to modify the compound of Daly et al. to obtain the instant compounds. Because Compounds that differ only by the presence or absence of an extra methylene group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methylene groups. See *In re Wood,* 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on 571-272-0867. The fax

phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NILOOFAR RAHMANI

12/10 /2007

/N/

/D.MARGARET SEAMAN/

PRIMARY EXAMINER

GROUP 1625